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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,472	04/25/2005	Gerard Griffioen	50304/068001	5411

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EXAMINER	
JOIKE, MICHELE K	

ART UNIT	PAPER NUMBER
1636	

NOTIFICATION DATE	DELIVERY MODE
08/07/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/527,472	GRIFFIOEN ET AL.	
	Examiner	Art Unit	
	MICHELE K. JOIKE	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-23* is/are pending in the application.

4a) Of the above claim(s) *22 and 23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 March 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/3/05, 11/9/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I in the reply filed on April 10, 2008 is acknowledged. The traversal is on the ground(s) that US2006/0068472 does not break unity because the reference does not teach that the yeast strain lacks a functional caspase gene, but only that caspase function is inhibited. This is not found persuasive because although US 2006/0068472 does not teach a yeast strain that lacks a functional caspase gene, it does teach that caspase function is inhibited, and Madeo et al teach a yeast strain with a non-functional caspase gene (see below). Together, the references teach claim 14. Therefore, unity is broken.

The requirement is still deemed proper and is therefore made FINAL.

Claims 22 and 23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on April 10, 2008.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. The hyperlink is found on page 3.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 14, 16-18, 20 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 2006/0068472 in view of Madeo et al.

US 2006/0068472 (see paragraphs 41, 81, 134, 233, 243 and 245 and Table 1) teach that Parkinson's disease affects about half a million individuals in the United States and previously has been considered a nongenetic disorder. Two genes are clearly associated with the disease: alpha-synuclein (PARK1) and parkin (PARK2). Insights into the role of toxic proteins in neurodegenerative disease suggest rational approaches to treatment. First, blocking the expression

or accelerating the degradation of the toxic protein can be an effective therapy. Because fragments of the toxic proteins may be more pathogenic than the full-length protein and specific cellular localization may enhance toxicity, blocking proteolytic processing and intracellular transport are reasonable approaches to treatment. Other therapeutic strategies include inhibiting the tendency of the protein to aggregate (either with itself or with other proteins), up-regulating heat shock proteins that protect against the toxic effects of misfolded protein, and blocking downstream effects, such as triggers of neuronal apoptosis. Overexpression of heat shock protein can reduce the toxicity of both mutant polyglutamine and mutant alpha-synuclein and caspase inhibition can reduce the toxicity of both polyglutamine and mutant SOD, indicating that therapeutic interventions of this type may apply across multiple neurodegenerative diseases. Although a yeast strain lacking a functional caspase gene is not taught, the reference teaches inhibiting caspase function. Pharmaceutical screens are now under way to identify agents that block the expression or alter the processing and aggregation of the toxic proteins responsible for neurodegenerative disease, or mitigate the harmful effects of these proteins on neuronal function and survival. The host cell used for expression can be yeast. It can be transformed with a gene encoding an amyloidogenic protein, for example, torsin. However, genes in Table 1 can also be used, including alpha-synuclein.

However, it does not teach a yeast strain lacking a functional caspase gene.

Madeo et al (Molecular Cell, 9: 911-917, 2002, specifically p. 916) teaches a yeast strain with a disrupted YCA1 (caspase) gene.

The ordinary skilled artisan, desiring to use a yeast strain lacking a functional caspase gene, would have been motivated to combine the teachings of US 2006/0068472 teaching a yeast strain transformed with an amyloidogenic protein, and a screening method to identify agents that block the expression or alter the processing and aggregation of the toxic proteins with the teachings of Madeo et al teaching a yeast strain with a disrupted YCA1 because US 2006/0068472 states that determining the mechanisms of toxicity of misfolded proteins remains the most important unresolved research problem for neurodegenerative diseases. It would have been obvious to one of ordinary skill in the art to use a yeast strain lacking a functional caspase because Madeo et al teach that the more simple yeast system may be better suited to resolve the order of some of the events in the apoptotic cascade. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over US 2006/0068472 in view of Madeo et al as applied to claims 14, 16-18, 20 and 21 above, and further in view of Poleev et al.

US 2006/0068472 teaches all of the limitations as described above.

However, it does not teach using a minigene.

Madeo et al teach all of the limitations as described above.

However, it does not teach using a minigene.

Poleev et al (Eur. J. Biochem. 267: 4002-4010, 2000, specifically pp. 4002-4003) teach using a minigene to encode the amyloidogenic protein, APP.

The ordinary skilled artisan, desiring to use a minigene would have been motivated to combine the teachings of US 2006/0068472 teaching a yeast strain transformed with an amyloidogenic protein, and a screening method to identify agents that block the expression or alter the processing and aggregation of the toxic proteins with the teachings of Madeo et al teaching a yeast strain with a disrupted YCA1, with Poleev et al teaching using a minigene to encode the amyloidogenic protein, APP, because US 2006/0068472 states that determining the mechanisms of toxicity of misfolded proteins remains the most important unresolved research problem for neurodegenerative diseases. It would have been obvious to one of ordinary skill in the art to use a minigene because Poleev et al teach that minigenes allow for several forms of mRNA, and because of this, sequences regulating neuron-specific splicing have been found. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over US 2006/0068472 in view of Madeo et al as applied to claims 14, 16-18, 20 and 21 above, and further in view of White et al.

US 2006/0068472 teaches all of the limitations as described above.

However, it does not teach using metal ions in the culture medium.

Madeo et al teach all of the limitations as described above.

However, it does not teach using using metal ions in the culture medium.

White et al (J. Neurochemistry 76: 1509-1520, 2001, specifically pp. 1509-1510) teach using metal ions in the culture medium.

The ordinary skilled artisan, desiring to use metal ions in the culture medium would have been motivated to combine the teachings of US 2006/0068472 teaching a yeast strain transformed with an amyloidogenic protein, and a screening method to identify agents that block the expression or alter the processing and aggregation of the toxic proteins with the teachings of Madeo et al teaching a yeast strain with a disrupted YCA1, with White et al teaching using metal ions in the culture medium, because US 2006/0068472 states that determining the mechanisms of toxicity of misfolded proteins remains the most important unresolved research problem for neurodegenerative diseases. It would have been obvious to one of ordinary skill in the art to use metal ions in the culture medium because White et al teach that metal ions such as copper and iron may be the source of increased free radical generation in neurodegenerative diseases. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be

considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Allowable Subject Matter

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHELE K. JOIKE whose telephone number is (571)272-5915. The examiner can normally be reached on M-F, 9:00-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michele K Joike, Ph.D./

Michele K Joike, Ph.D.
Examiner
Art Unit 1636